# SURVEILLANCE AND CONTROL OF EPIDEMIC KERATOCONJUNCTIVITIS

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ABSTRACT

*Purpose:* The purpose of this study was to determine if the implementation of a formal set of infection-control policy and procedures (ICPPs) can reduce the number of outbreaks of epidemic keratoconjunctivitis (EKC) and the number of nosocomially infected patients in a large teaching eye institute.

*Methods:* A retrospective and prospective study of the incidence of EKC and the number of affected patients was performed for the years 1984 through 1991. Infection-control measures (ICPPs) were formulated in 1992 with regulations implemented for patient control and management, hand washing, instrument disinfection, medication distribution, and employee furloughs. Two levels of ICPPs were established on the basis of nonepidemic or epidemic conditions. After implementation of ICPPs, a prospective 4-year study (1992 through 1995) and statistical analysis were performed to determine whether the number of outbreaks of EKC and affected patients significantly decreased.

*Results:* The incidence of institutional EKC epidemics per year was at least one and as many as three from 1984 through 1991. After implementation of a formal set of ICPPs, no epidemics occurred in 2 of 4 years studied. The number of epidemics and affected patients was significantly less when the years before and after implementation of ICPPs were compared by chi-square analysis ($P<.01$ and $P<.01$, respectively).

*Conclusions:* In this first prospective study of institutional outbreaks of EKC, the implementation of ICPPs was demonstrated to be an effective means to decrease the number of EKC outbreaks and nosocomially infected patients for this particular institution. Although several reports of institutional outbreaks of EKC have described infection-control measures that eventually controlled an outbreak well under way, this study provides policies and procedures that may effectively decrease the number and size of nosocomial epidemics of adenoviral conjunctivitis in large teaching eye institutions.

## INTRODUCTION

Epidemic keratoconjunctivitis (EKC) has been recognized for a century as a nonpurulent conjunctivitis associated with a characteristic keratitis that can spread rapidly within a community. Outbreaks have been reported in health-care settings, many in eye clinics where morbidity and lost productivity were considerable owing to the usually large number of affected individuals. Epidemics have been studied to determine clinical symptoms and signs, risk factors for transmission, and, with the identification of adenovirus as the etiologic agent, serologic types. Epidemiologic studies of several outbreaks of EKC in large eye clinics and hospitals have demonstrated that infection-control measures alone, such as strict hand washing, instrument disinfection, and prevention of medication contamination, were insufficient to prevent nosocomial transmission during an outbreak. These large institutional outbreaks were brought under control only when strict quarantine of affected patients was undertaken. However, to date, no study has demonstrated that the implementation of a formal infection-control policy in a large teaching eye clinic decreases the number and/or the severity of outbreaks of EKC.

In this prospective study by the author, the following hypothesis was tested: *Can the implementation of infection-control policies and procedures (ICPPs) decrease the incidence of nosocomial outbreaks of EKC in a large teaching hospital?* The number of epidemics and patients with nosocomially acquired EKC in a teaching eye clinic were documented over a 4-year period. After implementation of ICPPS, involving mandatory staff education, strict infection-control measures, and routine patient isolation, outbreaks and the number of affected patients were prospectively studied for an additional 4 years.

This prospective study was designed to test whether the development, incorporation, and monitoring of enforced ICPPs within a large teaching eye hospital and clinic could reduce the number and severity of nosocomial institutional outbreaks and much of the morbidity and suffering associated with this often iatrogenic disease. The implementation and monitoring of successfully tested ICCPs could be used in other teaching eye centers, satellite clinics, and/or private ophthalmologic offices as a means to limit nosocomial outbreaks.

## HISTORICAL REVIEW

In 1889, Ransohoff[1] described a patient who had been treated since 1881 for recurrent epiphora and eye pain. The patient had bilateral corneal

infiltrates, eight to ten in number, that were superficial and nonconfluent. Later that year, von Stellwag[2] and Fuchs[3] referred to Ransohoff's patient when they described an epidemic of conjunctivitis that had swept through Austria and produced a similar punctate keratitis. Von Stellwag treated several patients who initially presented with pain around the eyes and conjunctival dilation and inflammation. Round or oval infiltrates of the cornea would later appear; they were located centrally or in the periphery, sometimes in clusters, and occasionally one on top of the other in the superficial cornea. After administering cocaine anesthesia, von Stellwag obtained a corneal scraping for histopathologic examination. Although no bacteria were associated with the lesions, inflammatory cells were present. Von Stellwag called this disease *keratitis superficialis*.

Within several months, Fuchs[3] reported his descriptions of other patients with this disease. In an address to his colleagues in Vienna, Fuchs acknowledged the clinical descriptions of Ransohoff and von Stellwag and further characterized the manifestations of this new disease that he had observed in 36 patients. Characteristic symptoms were usually pain and photophobia. In all patients, an acute conjunctival inflammation developed without mucus or purulence, but with marked fluid secretion. Some patients were found to have conjunctival follicles. Early in the course of the conjunctivitis, after some 3 to 4 days, the small punctate lesions (punctiform) resolved and were replaced by larger lesions (flecken), usually more than 20 and sometimes as many as 100 in number. By scraping the epithelium and noting that the lesions remained, Fuchs demonstrated that flecken were not in the epithelium but were subepithelial. Flecken remained in the cornea for at least a year and were found to change in distribution. Men and women were equally affected. The lesions could be round, oval, or irregular in shape. Fuchs termed this disease *keratitis punctata superficialis*. Von Reuss[4] and Adler[5] published similar descriptions of this epidemic in 1889, referring to the characteristic corneal lesions as *keratitis maculosa* (von Reuss) and *keratitis subepithelialis* (Adler).

Between January and April 1901, near Bombay, India, Herbert[6] described an outbreak of over 200 cases meeting Fuchs' description of superficial punctate keratitis. Most cases involved a unilateral conjunctivitis that developed minute, faintly opaque infiltrates which caused the cornea to appear rough and pitted. Herbert also described small, round follicles of the upper tarsus with thickening of the limbal conjunctiva and ciliary and conjunctival injection. In performing bacteriologic studies of the corneal lesions, Herbert described encapsulated bacilli. Attempts to grow an organism in culture were unsuccessful, however. Inoculation

experiments were performed by taking mucoid discharge from the affected eye of a patient and placing it in the unaffected eye. No change occurred. Experiments were also performed by taking positive bacterial cultures grown from the eye of an affected patient and inoculating the eye of a healthy hospital attendant. Several days later a conjunctivitis appeared, but it was purulent and did not produce the clinical signs of keratitis punctata.

In 1909, Weiner[7] described the first case of keratitis punctata superficialis, as described by Fuchs, in the United States. His patient was a young woman who presented with about 30 small, round, grayish dots, averaging about 1 mm or less in diameter, in only one eye. Weiner proposed that the disease was due to "catarrh of the air passages." This case presentation, according to Weiner, must be rare because neither he nor his partner in their wide experience had ever noted a similar case.

The first epidemic in the United States was reported in Michigan .[8] In 1939, Hobson[9] described an outbreak of 16 cases in a Veterans hospital on the west coast. Through 1941, an epidemic was tracked from the Far East to Tasmania to Hawaii, where Holmes reported some 10,000 cases that began in the Pearl Harbor naval shipyard and spread throughout Oahu. [10-12] In 1942, Hogan and Crawford[13] reported an outbreak at a naval shipyard in San Francisco, which they speculated originated from the epidemic in Hawaii. Although shipyard workers believed that the disease was related to welding, Hogan and Crawford, after studying 125 patients, concluded that the disease must involve an infectious agent. They noted that others who were not involved with shipyard work, such as townspeople and hospital workers, also presented with the disease. Hogan and Crawford concluded that the disease was spread by close contact, with direct transfer of the infectious agent. On the basis of clinical findings and the explosive outbreaks that could occur with the disease, they proposed *epidemic keratoconjunctivitis* as a more appropriate term for the disease. The agent was thought to survive for only short periods; otherwise, even larger numbers of individuals would be affected. The investigators suggested that patients contracting the disease should be isolated from fellow workers for at least 15 days or until the conjunctivitis cleared.

Hogan and Crawford described membrane formation in 17 of their 125 patients. The membrane usually appeared between the fourth and eighth day after onset of disease. The membrane was thin and "milky" in three cases, but in the others it extended into the caruncle and semilunar fold and became more dense and difficult to remove. Hogan[14] later described a physician with EKC in whom a pseudomembrane developed. Laibson and Green[15] described a patient with a pseudomembrane, and in

a histopathologic study they found numerous polymorphonuclear leukocytes and mononuclear inflammatory cells entrapped in an eosinophilic fibrillar meshwork. They observed that epidemics varied in the likelihood of producing membranes or pseudomembranes. Dawson and coworkers[16] reported that 9 of 15 patients with EKC had inflammatory membrane formation and 7 had linear superior tarsal conjunctival scarring. They suggested that conjunctival scarring resulted from organization of the membrane and that both membrane formation and conjunctival scarring were manifestations of severe disease.

The etiology of the conjunctival involvement was further elucidated by the finding of viral particles by Dawson and coworkers[16] and Segawa,[17] who used electron microscopy in the acute disease. Membranes and pseudomembranes, they postulated, may represent an intense inflammatory response to the replicating virions. Dawson and coworkers[16] also described two patients in whom persistent corneal erosions developed during the acute disease. Transmission electron microscopic examination of corneal specimens from affected patients demonstrated adenoviral-like particles, suggesting that subepithelial infiltrates of EKC were related to viral replication in the epithelium. The investigators agreed with the findings of Laibson and coworkers[18] that topical steroids suppressed these corneal opacities, supporting the view of Jones[19] that these opacities were due to an inflammatory response to the viral antigens.

The concept of viral replication in the corneal epithelium was bolstered when Boniuk and coworkers[20] isolated adenovirus type 2 from the cornea of a patient with chronic keratitis. In Verhoeff's initial description of the histopathology of subepithelial opacities,[21] inflammatory cells were noted to congregate around "nerve channels" that split Bowman's membrane. Vass[22] also noted pathologic changes associated with corneal nerves. However, in a histopathologic study of a lamellar keratectomy obtained from a patient some 2 years after resolution of an acute conjunctivitis,[23] a lymphocytic infiltrate, as well as fibroblasts with collagen deposition, was noted with no evidence of viral particles. This study suggested that subepithelial infiltrates were composed of not only inflammatory cells but some underlying fibrosis. The implication was that the infiltrate might resolve, but the scarring to some degree would remain.

Dawson and associates[24] definitively described the time course and clinical appearance of the corneal lesions, expanding on Fuchs' observations of the early superficial lesions (punctiform) and the later subepithelial opacities (flecken). These investigators characterized this viral disease as a diffuse epithelial keratitis that begins 2 to 3 days after the onset of conjunctivitis. About a week into the disease, punctate focal whitish gray opac-

ities appear. Two weeks after the onset, stromal opacification begins underneath the focal epithelial lesions. With time, the epithelial lesions fade, leaving subepithelial opacities, which may remain for some time. Lastly, small gray epithelial opacities were described in the third and fourth week of the disease. Other rare ocular clinical findings that have been associated with adenovirus 14 are acute dacryoadenitis and perivascular hemorrhages.[19]

**IDENTIFICATION OF THE INFECTIOUS AGENT**

Many early reports of outbreaks of EKC suggested that an infectious agent was responsible. Herbert,[6] in studying corneal scrapings from patients with epidemic conjunctivitis, later reported gram-negative bacilli, a finding subsequently confirmed by others.[25,26] However, many other investigators failed to recover a bacterial isolate when cultures were obtained from patients with the disease.[27,28]

Wright[29] suspected a viral etiology and was able to transmit the disease to five human volunteers after filtering corneal washings through Kitasato candles. He chose these small, porous candle tubes because of the minute volume of his sample and their ability to filter to 0.7μm. Hogan and Crawford[13] speculated that the cause of the disease was most likely a virus because of (1) bacteriologic studies that were almost universally negative, (2) Wright's inoculation experiments, (3) transmission of the disease despite the absence of bacteriologic findings, (4) rapid progression of clinical signs involving the lymphatics of the lids and conjunctiva, which is typical of viral infections, and (5) failure of the infiltrates to ulcerate, which is typical of bacterial infections.

Sanders and colleagues[30-32] studied an outbreak of EKC in New York in 1942 in which a number of patients had headaches and several severely affected individuals had central nervous system symptoms such as protracted drowsiness. Sanders reported that he had isolated the etiologic agent; he said that neutralizing antibodies to the EKC virus had been identified that persisted in the convalescent sera of affected patients. One patient who volunteered to be inoculated with the Sanders virus manifested a conjunctivitis but no keratitis. This finding, coupled with the CNS symptoms of some of the patients in 1942, led to a suspicion that the St Louis encephalitis virus might be responsible for EKC. However, Cockburn and coworkers[33] studied two outbreaks of EKC and performed neutralization tests against St Louis encephalitis virus and the EKC strain of Sanders. No relationship between the St Louis encephalitis and the Sanders EKC viruses could be found.

Sanders later reported that the virus associated with EKC could not

be neutralized by antiherpes serum. However, Maumenee and coworkers[34] reported that the EKC virus and the herpes virus were similar in their crossed immunologic reactions. Investigators as early as Fuchs[3] had recognized that herpetic keratoconjunctivitis resembled EKC. The rapid onset of a follicular conjunctivitis with a punctate epitheliopathy was a well-recognized feature of both diseases. Jancke,[35] however, in a thorough study of the two diseases, concluded that EKC could not be caused by the herpes virus because EKC was not associated with vesicular eruptions, was usually bilateral, could not transmit herpetic disease in inoculated animals, and was not associated with corneal anesthesia.

In 1953, Rowe and coworkers[36] were studying the growth of cell cultures from adenoids removed from young children. During the first week, the cell cultures demonstrated sheets of normal-appearing epithelium. However, from 2 to 3 weeks after the cell cultures were started, the epithelial cells changed to morphologically distinct, large, round cells with clear peripheral cytoplasm and a densely granular center. The culture fluid was transferred to fresh cultures of adenoid, human embryonic tissue, and HeLa cells. In nearly every case, the same characteristic cellular changes were noted. Hyperimmunization of rabbits with the presumed agent-containing culture fluid produced neutralizing antibodies to the agent in culture. Some human sera provided neutralizing capacity, and others did not. The investigators designated this presumed virus "adenoid degeneration agent."

In early 1954, a 2-year-old girl with rhinitis, pharyngitis, and conjunctivitis was extensively evaluated for her respiratory illness at the National Institutes of Health.[37] During her admission she coughed in the face of her attending physician and the pediatric nurse, both of whom became ill 8 days later with a pharyngitis. The physician also developed rhinitis and a unilateral conjunctivitis. Five additional staff and other pediatric patients were later affected. Serologic studies identified the presumed causative agent as type 3 adenoidal-pharyngeal-conjunctival virus. Rowe and associates.[8] had identified the prototypical viruses for types 1 and 2 from surgically removed adenoids. The prototypical type 3 virus was isolated from a young volunteer with a common cold who underwent nasal washings.[39] These agents were termed collectively the adenoidal-pharyngeal-conjunctival, or APC, group of viruses.[40]

In 1954, Ryan and coworkers[41] described a laboratory technician who was accidentally exposed while working with type 3 adenovirus. The technician developed a uniocular, acute follicular conjunctivitis without corneal involvement but with a sore throat. Cultures from the affected eye were positive for APC type 3. The investigators also reported a pediatri-

cian who developed a follicular conjunctivitis, rhinitis, and pharyngitis after a sick child coughed in his face. Three children and three adults also exposed to the sick child developed a pharyngitis and rhinitis, and four developed a conjunctivitis. The cornea was not affected. In a study of an outbreak of some 400 cases of this newly recognized disease—pharyngoconjunctival fever—the disease was found to be highly infectious in children; adults were more likely to be immune, presumably because of previous exposure.[42,43] Contaminated swimming pools were found to be a source for the infection, which nearly always produced a systemic illness that could manifest as a nasopharyngitis, fever, gastritis, and lymphadenopathy. The conjunctivitis was usually acute, follicular, and nonpurulent. It could be bilateral. The disease had an incubation period of 5 to 10 days and lasted from 1 to 2 weeks. In a Canadian study of pharyngoconjunctival fever,[44] the corneal involvement varied from transient epithelial opacities to infiltrates similar to those noted in EKC. All opacities disappeared within 6 months, however. The constitutional signs and symptoms with the variable and fleeting nature of the corneal opacities distinguished this disease entity from EKC, a disease whose etiology was as yet unknown.

Two years later, Jawetz and coworkers[45-50] studied a merchant seaman who traveled from the Far East to San Francisco, presenting to the eye clinic with a severe conjunctivitis. The patient, identified as "Trim," developed subepithelial infiltrates characteristic of EKC after a severe conjunctivitis with pseudomembrane formation. The virus was cultured, and cytopathogenic effects in HeLa cells were similar to those noted with the APC viruses but did not fit into an established type. The cytopathogenic effects were neutralized by serum from patients with EKC and not by antiserum to the herpes simplex virus, antiserum to the St Louis encephalitis virus, or monotypic antisera to types 1 through 7 of the APC group of viruses. Fluid from the HeLa cell cultures infected with the EKC virus fixed complement with antiserum to the APC viruses, indicating that the EKC virus was a member of the APC group, later specified as type 8.

Patient Trim was attended to by nurse "Cott" while hospitalized. Ten days after attending Trim, Nurse Cott developed an acute conjunctivitis with enlarged preauricular nodes. Subepithelial opacities gradually developed, with a markedly elevated serum antibody titer rise to "virus Trim." Thus, the first nosocomial case of EKC was identified and documented.

To establish conclusively that this newly discovered APC virus was responsible for EKC, Mitusi and coworkers[51] inoculated five Japanese volunteers with the Trim virus supplied by Jawetz. Following administration of a local anesthetic, the upper fornix of the conjunctiva was scraped light-

ly with a sharp knife. An inoculum was instilled onto the conjunctiva five times at 5-minute intervals. A control inoculum was introduced onto the other eye. In three subjects, an acute follicular conjunctivitis developed with preauricular adenopathy, and subepithelial keratitis developed about 1 week after onset of the conjunctivitis. Viral cultures resulted in recovery of the virus in all three cases. In the fourth subject, a mild conjunctivitis developed but no keratitis. In the fifth subject, disease did not develop, not even a mild form, despite repeated inoculations. Serologic studies indicated that this volunteer had partial immunity.

By common agreement, the investigators studying the adenoid-degenerating, APC, respiratory illness, and acute respiratory disease viruses decided to designate this group of viruses the adenoviruses.[52] This group had in common the ability to cause unique cytopathogenic changes in cell culture and nonpathogenicity for ordinary laboratory animals. The viruses were heat-labile, filterable, and ether-resistant and had soluble, group-specific, complement-fixating antigens that were not type-specific.

Adenovirus type 8 was the only reported causative agent in outbreaks of EKC around the world until the early 1970s, when adenovirus 19 emerged as another major cause of the disease in the eastern United States, Canada, and Europe.[53-61] The virus was first isolated by Bell and coworkers[62] in Saudi Arabia while they were studying the role of viral infections in trachoma. Viral cultures were performed on large numbers of children and adults. An unknown virus was isolated from conjunctival scrapings of a young child that was later serotyped as adenovirus 19. The first reported outbreaks of EKC due to type 19 were reported in 1974 in several eastern US states.[56-58] An outbreak in Tennessee involved a mixed infection of 145 patients. Adenovirus type 8 was isolated in 62% of the cases and type 19 in 28%. The two viruses were indistinguishable in their clinical manifestations and secondary household attack rates.

For some as yet unexplained reason, some other adenoviral types produce epidemics that resemble in nearly all aspects the clinical features of EKC, including the corneal lesions.[63-66] One of the best examples was an outbreak in Bristol, England, of 113 cases due to adenovirus type 4.[65] Even though the disease was not as severe as in outbreaks of EKC due to adenovirus types 8 and 19, the cornea was involved in nearly 25% of cases and subepithelial opacities developed in 15%; all but two cases resolved in 1 month. Type 4 adenovirus was also noted to produce relatively severe disease in an outbreak of mixed infection with type 8 in Taiwan.[66] However, type 4 adenovirus is usually associated with respiratory infections and occasional outbreaks of pharyngoconjunctival fever associated with swimming pools.[67]

In 1976, Schaap and coworkers[68-69] reported the isolation of a new type of adenovirus involved in a major outbreak of EKC in Holland. This serotype has been designated adenovirus 37 and has been implicated in many outbreaks throughout Europe and the United States.[70,71] Using DNA restriction analysis, Kemp and associates[72] studied strains of adenovirus types 19 and 37 isolated and collected from cases of EKC over a 10-year period in order to detect differences in antigenic and restriction enzyme patterns. Thirty-five percent of the isolates recovered between 1973 and 1981 and typed by hemagglutination-inhibition tests as adenovirus 19 were, in fact, adenovirus 37. The earliest case of type 37 was identified in 1976, and since 1977 it has been a major cause of EKC. Strains intermediate between types 8, 19, and 37 suggesting that any one type evolved from the other were not identified. The investigators suggested that these viruses arose by recombination rather than through some other genetic mechanism. Immunologic pressure would not be sufficient to cause the production of these new types so quickly. Adenoviruses use a replicative mechanism that is conducive to recombination. During replication, a single-stranded DNA molecule is formed from the parental virus, which may hybridize efficiently with a strand from a second virus that may have coinfected the cell. If this study is correct about the evolutionary rate of adenoviruses, the discovery of yet new types in the near future would not be a surprise.

#### EPIDEMIOLOGY OF EKC OUTBREAKS IN EYE CLINICS

Outbreaks of EKC were certainly perpetuated by early physicians who treated the disease unaware of its communicability. Hobson[9] reported an outbreak within a hospital setting, and despite its affecting two members of the staff, ward attendants, and patients who were all living on the hospital grounds, he concluded that the disease was not contagious but was related to allergy. Hogan and Crawford[13] noted that even though most of their patients worked in the shipyards, others were hospital employees.

Cockburn and coworkers[33] noted in a study of an outbreak of nine cases of EKC that all patients had attended a particular glaucoma clinic. In the 2-month period of the outbreak, a total of 40 patients had been examined in the glaucoma clinic. Assuming that the disease was caused by a contagious infectious agent, the calculated attack rate was about 25%. The investigators speculated that the possible mechanisms of infection were finger-to-eye transmission by the physician, tonometer and/or various other instruments, and towels. Because the tonometer had been used on all patients with glaucoma and only this group became infected, the investigators concluded that this was the likely mode of transmission. In

studying the outbreak in detail, however, Cockburn and coworkers noted that on each day that a patient was presumed to have been infected, another patient with symptoms of keratoconjunctivitis had attended the clinic. Furthermore, the infected and presumably inoculated patients not only had been tested with the same tonometer, but also had been examined by the same physician. The tonometer and the physician were clearly implicated in transmitting the disease. The disease was halted when the clinic physicians were made aware of their possible role in transmitting the infection and disinfection of the tonometer was routinely performed. The investigators also concluded that specialty clinics were at particular risk for spreading the disease because of the likelihood that they would serve as a primary focus of the infection, with transmission of the disease to referring doctors and clinics creating secondary foci in the community.

Thygeson[73] studied EKC that involved 32 physicians and 40 nurses. He observed that because these health-care personnel frequently rubbed their eyes, finger-to-eye transmission could be a mode of inoculation. The physicians agreed that the likely cause of their infections was finger-to-eye transmission, since they could recall no other risk factors for the disease. Thygeson also suggested that tonometry and contaminated solutions were involved in transmitting EKC. Trauma, especially the removal of foreign bodies from the cornea, was observed to be associated with the disease. However, in many cases no trauma had occurred. Thygeson made the following recommendations for prevention of EKC: (1) discarding all dropper bottles, (2) using individual sterilizable droppers, (3) washing the hands adequately with soap and water before and after treatments, (4) sterilizing tonometers and all other instruments used on the eye, and (5) recognizing and isolating cases early.

Dawson and Darrell[74] reported an epidemic involving 26 patients treated by an eye, ear, nose, and throat specialist who was infected. None of the 50 patients treated for otolaryngologic problems developed EKC. However, of the 98 patients subjected to ophthalmic procedures, 21 developed the disease, an attack rate of 21.4%. Tonometry was implicated in transmitting the disease, with an attack rate of 74%. Therapeutic drops, minor procedures, and slit-lamp examination also carried high attack rates (45%, 38%, and 20%, respectively).

In a study of schoolchildren in the community during the outbreak studied by Dawson and Darrell, EKC was diagnosed and adenovirus type 8 was recovered.[75] Mitusi and coworkers[76] described atypical adenovirus type 8 infections in Japanese children, manifested by fever, malaise, gastrointestinal and upper respiratory symptoms, and conjunctivitis. Transmission within a family was documented. Dawson and coworkers[75]

recognized that children with relatively mild disease transmitted EKC more readily than adults with severe conjunctivitis. In the Far East, a large percentage of children and adults were found to have serologic evidence of previous infection.[77] In the United States, however, neutralizing antibodies to adenovirus type 8 were found in less than 5% of adults.[75,78] Thus, many susceptible people are at risk for infection in the United States

Dawson and Darrell[74] concluded that the epidemic under study had originated in an endemic population of schoolchildren and was then transmitted to their parents, who introduced the disease into an eye clinic, where the disease was transmitted by direct contact between a physician and susceptible patients. Further study of the schoolchildren with disease revealed that many were coinfected with *Haemophilus aegyptius* (Koch-Weeks bacillus). These bacterial infections were known to be seasonal, and outbreaks of EKC had been postulated to be more likely during simultaneous infections because of the copious conjunctival discharge produced by *H aegyptius*. Bell and associates[62] studied bacterial and viral cultures in a large population in Saudi Arabia and also noted seasonal variations in recoverable adenovirus.

Laibson and coworkers[79] described an outbreak of 102 cases of EKC at a large teaching eye hospital over an 8-month period. Fifty cases were community-acquired and 52 were nosocomial. The prolonged nosocomial transmission was determined to result from contact between physicians in the prodromic stage of the disease and susceptible patients. Despite the institution of rigid infection-control measures, such as discontinuation of routine tonometry, identification and isolation of all patients suspected of having EKC on entering the clinic, and education of residents and staff about rubbing or touching their eyes, nosocomial spread of the disease continued. A large number of hospital staff were infected, including eight residents and three nurses. In 13 of the nosocomial cases, patients had contact with residents who subsequently developed the disease. The investigators speculated that if hospital personnel who developed the disease had voluntarily relieved themselves of duty, the number of nosocomial cases could have been reduced.

Dawson and associates[24] studied an outbreak that began in the emergency department, where an infected patient was examined by three residents and one staff physician. Seven of 38 patients subsequently examined that day developed the disease. Only 2 of the 7 infected patients were exposed to the Schiotz tonometer. The physicians' hands were suspected in the inoculation of the susceptible patients. The recommended preventive measures were thorough hand washing with soap and water before patient examination, thorough cleansing of contaminated instruments,

and, importantly, prohibition of health-care workers with EKC from contact with patients for at least 2 weeks from onset of the disease.

Sprague and colleagues[80] reported an industrial outbreak in 114 workers. The disease was transmitted by a contaminated ophthalmic eyewash and by finger-to-eye transmission by the nursing staff. After the dispensary was closed and careful aseptic techniques were employed by the ophthalmologists, the epidemic resolved. The investigators also speculated that minor trauma was important in establishing an infection. Removal of foreign bodies, a common occurrence in an industrial-setting dispensary, can provide optimal conditions for patient inoculation. Several investigators considered minor trauma to be involved in producing "shipyard eye." Indeed, Mitusi and associates[53] and Bietti and Bruna[81] demonstrated that disease transmission was more effective by first abrading the conjunctiva and then inoculating the virus. The inoculum for both investigations was provided by Jawetz.

Use of the tonometer is undoubtedly involved in the transmission of EKC.[33,73] This is the instrument that most commonly comes in contact with the ophthalmic patient, often resulting in minor disruption to the corneal or conjunctival epithelium. Newer types of tonometry have also been implicated. In a case-control study of an outbreak in an eye clinic in January 1988,[82] an epidemic was associated with exposure to pneumotonometers and one particular provider. The clinic had instituted the infection-control procedures recommended by the manufacturer and used 70% isopropyl alcohol wipes. This method appeared to be inadequate, owing either to ineffective eradication of the virus or to the inability to disinfect the entire area of the instrument that came in contact with the patient or the physician. The investigators recommended the complete abandonment of pneumotonometry during an EKC outbreak.

The general population is increasingly aware of the risk of nosocomial infections when seeking medical care.[83] In one outbreak studied by the Centers for Disease Control and Prevention (CDC) in Atlanta, a patient called the public health authorities to complain that he and his spouse had developed a conjunctivitis after having been examined by the same ophthalmologist.[84] An epidemiologic investigation by the public health authorities determined that 39 patients had developed EKC in this particular outbreak. A case-control study traced the risk factors for transmitting the disease to an examination by one of the four ophthalmologists in the group and to procedures such as tonometry or removal of a foreign body.

Recommendations by the investigators from the CDC included (1) hand washing, (2) instrument cleaning, (3) isolation of infected patients, (4) discarding of open ophthalmic solutions, (5) postponment of elective

procedures, and (6) patient education about measures to decrease the risk of secondary transmission.

Recent reports of outbreaks in ophthalmology clinics have demonstrated varying degrees of success in preventing nosocomial spread of EKC. A large outbreak of EKC due to adenovirus 8 occurred at the Illinois Eye and Ear Infirmary for 6 months in 1985 and involved 401 patients; 110 cases were nosocomial.[85] Initial routine infection-control efforts to curtail the outbreak were unsuccessful. The epidemic was not brought under control until all patients were examined for possible infection upon entering the clinic. Specially trained nurses were used for triage. To facilitate the triage, all clinic entrances except one were blocked. Anyone suspected of having conjunctivitis was triaged and sent to a special room, where a more thorough examination and assessment of the patient's condition could be done without risking the inoculation of other patients.

An outbreak of EKC at a military base in the Philippines involved some 2,600 cases of adenovirus types 8 and 19 and enterovirus.[86] The number of cases represented 18% of the active-duty military personnel, a sufficient number to impair seriously the military preparedness of the base. In an effort to minimize the spread of the disease, strict isolation of infected personnel was undertaken, which included a conjunctivitis clinic located in a tent that was physically separated from the base hospital, and for those infected, separate living, dining, and bathing facilities, isolation from the workplace, and restricted travel. Public education about the risk factors for the disease was attempted through newspaper and television announcements.

An epidemic at the University of Virginia Ophthalmology Clinic from July to September 1986 involved 126 patients.[87] Risk factors and mode of transmission for the disease were studied by comparing cases and controls for exposure to risk factors. Pneumotonometry, multiple clinic visits, and contact with a contaminated physician were significant risk factors for producing nosocomial disease. The outbreak presumably resulted from inadequate instrument disinfection and finger-to-eye transmission by physicians. Studies of adenoviral contamination of several patients' hands and disinfection with soap and water revealed that residual virus could still be cultured. Recommendations included the wearing of gloves for examining the eyes of patients with EKC. In addition, it was advised that infected ophthalmologists be furloughed until no further risk of transmission existed.

## MATERIALS AND METHODS

A retrospective and prospective study of nosocomial outbreaks of EKC at a large teaching eye institute was undertaken by the author. The study aims were to gather data on the frequency of outbreaks, to determine risk factors contributing to the initiation and spread of the disease, to formulate ICPPs that could be implemented by the Institute-at-large to control and prevent epidemics, and to determine if implemented ICPPs could decrease the incidence of EKC outbreaks and nosocomially infected patients at the Institute.

The author convened an Infection Control Committee (ICC) to coordinate the numerous hospital and clinic personnel who would be involved in an integrated infection-control effort and to build a consensus about policy and procedures that could readily be implemented and would conform to the rules and regulations of the hospital and the Institute. The author chaired the Committee, which consisted of the Chief of the Infection Control Department of the Hospital, the Infection Control Practitioner (ICP) of the Hospital, the director of nursing at the Institute, and the heads of nursing of the emergency department, the operating room, and floor services. After convening of the ICC for 2 years and after the implementation of ICC policy and procedures, other ophthalmologists were invited to serve on the ICC; these persons could be called on to serve as acting chairperson for Condition Red when the author was unavailable or out of town. Two members of the cornea and external disease staff were asked to attend meetings of the ICC, and each served once as acting chair of the ICC during an epidemic. The ICC met monthly when there were no outbreaks and weekly during outbreaks. When outbreaks had not occurred for 2 successive years, the ICC met once every 3 months.

The stated purpose of the ICC as defined by the author was to formulate policy and procedure to prevent EKC outbreaks at the Institute if possible and to contain outbreaks once they occurred. Formulation and coordination by the author of policy and procedure was based on (l) a literature review by the author of EKC and the reported management of outbreaks, (2) experience with managing outbreaks at the Institute, including assessments and written reports made by the Infection Control Department of the Hospital and Department of Health and Mental Hygiene (DHMH) of the State of Maryland, (3) input from members of the ICC, the departmental chairman, and invited guests to the ICC, and verbal or written input from faculty, staff, and residents, and (4) consideration of the physical plant, including floor plans and patient flow from the departmental administration.

The author gathered experience with EKC at the Institute from four sources: (1) Maumenee's response to Thygeson's experience with EKC,[88] (2) anecdotal recollections of outbreaks and sources from former chairmen and faculty, (3) reports of outbreaks in the minutes of meetings of the Infection and Epidemiology Committee of the Johns Hopkins Hospital from 1980 to 1989, and (4) data collected weekly by the ICP on community and nosocomial cases occurring at the Institute from September 1989 to January 1996.

Floor plans and patient flow were reviewed with the Senior Administrator of the Institute and the head of patient relations. The need for patient safety and convenience was considered. Physical space for the Red Eye Rooms was designated according to ability to provide isolation, running water, adequate space, and convenience for the patient and the treating physician.

The pertinent literature was reviewed by the author and is summarized in the Historical Review section of this thesis.The pertinent literature was presented to the ICC for deliberation and review. The ICC deliberated for 6 months before issuing a formal infection policy and procedure statement that had been approved by the departmental chairman. The ICC realized that the policy and procedures would in all likelihood need revision once implemented and subjected to the day-to-day rigor of an outbreak. The policy and procedures were divided into two conditions of implementation. Condition Yellow was to be in effect at all times as a baseline state of alert. Condition Red was to be implemented if the Institute was at risk for an imminent outbreak or if an outbreak had been detected. The criteria for initiation of Condition Yellow or Condition Red were based on a review of the patterns of community cases of EKC presenting to the Wilmer emergency department and the relationship to outbreaks of nosocomial cases within the Institute.

#### EPIDEMIOLOGIC INVESTIGATION

Outbreaks of EKC were reported to the DHMH, where a formal investigation and reports were generated.[89-90] The epidemiologic investigations were assisted by the author and members of the ICC.

##### *Case Definitions*

A nosocomial case of EKC was defined as any patient in whom a resident or staff ophthalmologist diagnosed EKC as manifested by an acute onset of follicular conjunctivitis with preauricular adenopathy and the development of characteristic subepithelial infiltrates or a positive adenoviral culture. The patient was to have visited the Institute within the previous 21

days. A community-acquired case was defined with the same clinical criteria, except the patient had not visited the Institute within 21 days.

*Case Findings*

The ICP identified nosocomial and community-acquired cases by reviewing the emergency department and clinic charts. These cases were reconfirmed by the DHMH as nosocomial or community-acquired by a review of patient records and cross-checking of the hospital computerized patient log for prior clinic visits. The DHMH also performed an environmental investigation to assess the effectiveness of the ICPPs formulated and instituted by the ICC. Changes in infection control procedures were communicated to the DHMH by the ICP and by the Director of Infection Control of the Hospital.

*Case-control Study*

The ICC and the DHMH performed a case-control study in which two control patients were selected for each nosocomial case. Both controls were matched to the nosocomial case by date and place of the initial visit. One of the controls was selected to match the physician and one was selected to match the day of examination but a different physician. Because each physician used his or her own examining room on a particular day, controls that were matched by physician were also matched by examining room. Resident coverage of the emergency department usually involves one physician, so emergency department cases and their controls had the same physician.

*Case Investigations*

A questionnaire developed by the ICC and the DHMH was used for data collection. Patient charts for nosocomial cases and controls were reviewed. Data for community-acquired cases were obtained from the records kept in the emergency department. The investigation studied the following factors for all cases and controls: age, preexisting eye conditions, diagnosis at the time of initial visit, procedures at the initial visit and follow-up visits (eg, slit-lamp examination, tonometry), room used at initial visit, and physician and staff in contact with the patient.

*Statistics*

The epidemic rate (number of epidemics/total number of patient visits) and the affected patient rate (number of affected patients/total number of patient visits) were tested for significance by chi-square test of observed versus expected. The number of patient visits for the years 1984 through

1987 were calculated using the number of patients seen in 1988, because the data on patient visits from 1984 through 1987 were not available. The 95% confidence interval was based on a Poisson distribution. Statistics employed in the case-control study utilized the chi-square test for computing proportions. Odds ratios and 95% confidence intervals were calculated by the Cornfield method.

## RESULTS

### EKC AT THE INSTITUTE

*Outbreaks Up to 1948*

Maumenee reported in 1948 that he was unaware of any outbreaks of EKC in Baltimore.[88] Despite the number of outbreaks in the United States that had been reported by others during World War II, especially on the West Coast, Maumenee did not know of any epidemics but had occasionally diagnosed and treated sporadic cases. He remarked that, like Thygeson, he had noted the vulnerability of the eye-care provider's office to this disease, since he had treated three oculists with EKC.[88]

*Outbreaks From 1955 Through 1979*

As Director of the Wilmer Institute from 1955 through 1979, Dr. A.E. Maumenee recalled outbreaks occurring at least twice and occasionally three times a year. The outbreaks usually occurred in the Anterior Segment or Glaucoma Service, and the use of the Schiotz tonometer was usually implicated in the epidemics.

*Outbreaks From 1980 Through 1988*

Minutes of the Hospital ICC for the years 1980 through 1988 were reviewed for reports of outbreaks of EKC at the Institute. Between 1984 and 1988 (Table I) at least one epidemic per year at the Institute was recorded in the minutes of the Hospital ICC. In 1984, three epidemics were described: In June, 10 patients were identified with EKC; in October, 20 nosocomial cases were reported; and in December, 3 more cases. In January 1985, 7 nosocomial cases were reported. In June 1986, 7 nosocomial cases, all in patients seen by the same physician, were reported. In October through December 1987, two epidemics and 19 nosocomial cases were identified and two physicians were diagnosed as having EKC. In September 1988, an outbreak of 30 cases in the private clinic was described.

TABLE I. RETROSPECTIVE AND PROSPECTIVE STUDY OF EKC AT WILMER INSTITUTE BY NUMBER OF OUTBREAKS AND NUMBER OF AFFECTED PATIENTS.*

| RETROSPECTIVE YEAR | NO. OF EPIDEMICS | NO. OF PATIENTS | TOTAL NO. OF PATIENT VISITS |
|---|---|---|---|
| 1984 | 3 | 23 | — |
| 1985 | 1 | 7 | — |
| 1986 | 1 | 7 | — |
| 1987 | 2 | 19 | — |
| 1988 | 1 | 30 | 35,476 |
| **PROSPECTIVE YEAR** | | | |
| 1989 | 1 | 6 | 40,786 |
| 1990 | 1 | 6 | 40,867 |
| 1991 | 2 | 55 | 40,166 |
| ICPP Implemented | | | |
| 1992 | 1 | 7 | 47,363 |
| 1993 | 0 | 0 | 50,208 |
| 1994 | 0 | 0 | 52,773 |
| 1995 | 1 | 14 | 60,512 |

* Implementation of infection-control policies and procedures (ICPPs) in 1991 significantly decreased number of epidemics ($p<.01$) and number of affected patients ($p<.01$) compared with years 1984-1991 and 1992-1995.

*Outbreaks From 1989 Through January 1991*

An ICP was assigned to gather data on all cases of community-acquired and nosocomial EKC logged from September 1989 to January 1996 at the Wilmer Institute. Two nosocomial outbreaks were identified, one in September 1989 involving 6 cases and the other in December 1990 and January 1991 involving an additional 6 cases.

*Outbreak of March 1991*

An outbreak of nosocomial EKC occurred in March 1991, with 17 cases identified. After resolution of the epidemic, the author asked for and received permission from the departmental chairman to prospectively study whether the incidence of outbreaks of EKC and the number of nosocomially infected patients could be decreased by implementing for-

mal ICPPs formulated by an ICC. The author also asked for and received from the departmental chairman the authority to chair the ICC and the authority to implement and monitor ICPPs throughout the Institute when the ICPPs were approved by the ICC and the departmental chairman.

*EKC Infection Control Policy and Procedures Stemming From Outbreak of March 1991.* The author convened an ICC with the purpose of formulating the ICPPs on the basis of a review of the literature, past experience with EKC at the Institute, and input from the Hospital Infection Control faculty, staff, and administration. Implementation was to include holding semiannual Infection Control training sessions and providing disease updates in the community and the Institute.

To provide infection control of EKC, two levels of alertness (Condition Yellow and Condition Red) were specified, each indicating what appropriate actions were necessary to protect personnel, patients, and visitors at the Institute. Specific measures were enacted for each level of alertness such that an appropriate response could be made to prevent or limit an outbreak of epidemic adenoviral or keratoconjunctivitis. Condition Yellow (Table II) is a baseline level of alertness that is in effect at all times except during an actual or impending epidemic. It is a condition of caution that specifies infection control measures for the baseline, nonepidemic occurrence of viral conjunctivitis for patients or personnel presenting to the Institute. In Condition Red (Table III), the Institute is on full alert during a suspected outbreak, with staff and patients regularly presenting themselves to the Institute for evaluation of the disease and an extremely high likelihood of communicating the disease to other noninfected individuals.

A central component of the ICPPs is two dedicated rooms, the Red Eye Rooms, to be used only for the evaluation and treatment of patients with suspected viral conjunctivitis. One Red Eye Room is located in the emergency department area, and the other is adjacent to the Cornea service. These rooms contain dedicated equipment and supplies that provide for the evaluation and treatment of patients without the need to move to them other rooms or to share equipment and supplies. The Red Eye Rooms have waiting areas that are physically separated from other areas.

The specific infection control measures for each of the two levels of alertness for adenoviral conjunctivitis are (1) patient control and management, (2) hand washing, (3) instrument disinfection, (4) medication distribution, and (5) employee furloughs. These are described as follows:

*Condition Yellow*

A state of caution for the Institute in which ICPPs are implemented for

TABLE II: CONDITION YELLOW*

| |
|---|
| **PATIENT CONTROL** |
| No routine screening. Patient or staff with signs or symptoms of conjunctivitis to Red Eye Room. |
| **HAND WASHING** |
| Soap and water before and after each patient. |
| **INSTRUMENT DISINFECTION** |
| **Goldmann:** Wescodyne at least 10 minutes, rinsed, dried. |
| **Pneumotonometers:** Sterile probe caps discarded after each use. |
| **Tonopens:** Cover caps discarded after each use. |
| **Contact Treatment and Diagnostic Lenses:** Soaked in hydrogen peroxide for 10 minutes, rinsed, dried. |
| **Instrument Surfaces:** Wiping with Wescodyne at least once a day. |
| **MEDICATION DISTRIBUTION** |
| Drops are to be discarded and replaced at least once per month and whenever contamination is suspected. |
| **EMPLOYEE FURLOUGHS** |
| Employee with suspected viral conjunctivitis is relieved for 3 days, after which another evaluation is performed. If signs of disease continue, employee is furloughed until no drainage or for 2 weeks. |

* Infection-control policies and procedures in effect in nonepidemic states of alertness to provide infection control of EKC.

the everyday, baseline, nonepidemic occurrence of viral conjunctivitis for staff and patients.

(1) Patient control and management: During Condition Yellow, no routine screening will be performed on patients visiting the Institute; however, any patient who is noted by the professional staff to have signs and symptoms of conjunctivitis shall be referred to a Red Eye Room. If a diagnosis of nosocomial conjunctivitis is suspected, the case shall be logged and reported to the Infection Control Practitioner or the author as chairman of the Infection Control Committee.

(2) Hand washing: Hand washing with soap and water for at least 10 seconds is to be done before and after each patient, including each time gloves are removed after patient contact. Hands are to be dried with clean paper towels only. Any problems with supplies for hand washing should be reported to the Housekeeping Department. The Infection Control Department should be notified of any ongoing problems with the maintenance of adequate supplies.

(3) Instrument disinfection: The following instruments are considered highly likely to be involved in the transmission of adenovirus: Goldmann tonometer tip, pneumotonometer tip, pinhole/occluder, and instrument with surfaces contaminated with eye secretions.

(a) Disinfection of Goldmann tonometers: Goldmann tonometers may be disinfected with Wescodyne. The tonometers are placed in petri dishes with 13-mm holes drilled in the covers, with the tips of the tonometers extending at least to the first black line, and are soaked for at least 10 minutes. Upon removal for use, the tips are to be thoroughly rinsed with water or saline and dried with a clean tissue or gauze.

(b) Pneumotonometers are to be used with sterile tonometer probe caps, recognizing that accuracy of measurement may be affected by about 2 mm Hg. The probe caps are to be discarded after each patient measurement.

(c) Disinfection of Tonopens: Tonopen covers are to be discarded after each patient measurement. The hard surfaces of the instrument should be disinfected by wiping with Wescodyne after each patient use.

(d) Contact diagnostic and laser treatment lenses: Retinal and glaucoma lenses used for diagnostic and laser treatment should be soaked in hydrogen peroxide for at least 10 minutes. After soaking, the lenses should be thoroughly rinsed with water or saline and dried with a clean tissue or gauze.

(e) Instrument surfaces: All instruments surfaces contacted by either patients or staff (eg, slit-lamp knobs, handles, tables) are to be disinfected by wiping once each day and after any observed contamination by eye secretions. Hands must be washed (as previously described) after contact with instrument surfaces contaminated by eye secretions.

(4) Medication distribution: Dilating and other diagnostic drops are to discarded and replaced at least once each month and whenever contamination of the dropper tip is suspected.

(5) Employee furloughs: Infected employees are not to work in any patient care areas until symptoms are resolving and conjunctival drainage, whether clear or purulent, has stopped. This includes employees who work in patient care areas but do not have direct patient contact. After presenting to an ophthalmologist for an evaluation, employees with possible viral conjunctivitis will be relieved from duty for approximately 3 days, after which they will undergo another ophthalmologic assessment. Employees with continuing clinical evidence of infection will then be relieved from further duty until symptoms and drainage are resolving. Conjunctival cultures for adenovirus are to be obtained from all employees evaluated by the professional staff.

TABLE III: CONDITION RED*

| |
|---|
| **PATIENT CONTROL** |
| Designated health-care worker is situated at the entrance of Institute to screen all patients. Any suspect patient is taken to Red Eye Room. |
| **HAND WASHING** |
| Same as Condition Yellow. |
| **INSTRUMENT DISINFECTION** |
| Avoid all forms of tonometry except when medically necessary; all surfaces are to be disinfected at least three times per day. |
| **MEDICATION DISTRIBUTION** |
| All drops are to be discarded at the declaration of Condition Red. Drops are to be discarded daily in the ER and twice per week in the other clinics. |
| **EMPLOYEE FURLOUGHS** |
| The same as Condition Yellow, except staff with disease are automatically furloughed for 2 weeks. |

* Infection-control policies and procedures in effect when Institute is in an epidemic of keratoconjunctivitis or is in imminent danger of an epidemic.

*Condition Red*

A full alert for the Institute during a suspected outbreak in which staff and patients are regularly presenting to the Institute for an evaluation of the disease and the likelihood of communicating the disease to other noninfected individuals is extremely high. Condition Red is implemented when there is any evidence that two or more patients were infected during their visit to the Institute, or when 20 or more community-acquired cases are logged in the ER Red Eye Room in a single week. Reversion to the baseline Condition Yellow may occur when there is no evidence of ongoing nosocomial infection and when the weekly number of suspected cases as logged in the Wilmer ER Red Eye Room has dropped below 20.

(1) Patient control and management: A designated health-care worker will be situated at the entrance to the Institute to screen all patients as they arrive for registration. Any patient suspected of having infectious conjunctivitis will be referred to a separate registration desk and will be routed from there to one of the Red Eye Rooms. All other entrances to the Institute will be closed to routine patient access.

(2) Hand washing: Hand washing should be performed as specified as

under Condition Yellow. The Infection Control Department should be notified promptly of any problems with the maintenance of adequate supplies.
(3) Instrument disinfection: All forms of tonometry should be avoided during Condition Red unless medically indicated. Pneumotonometers are not to be used while Condition Red is in effect. All surfaces of instruments contacted by either patients or staff (eg, slit-lamp knobs, handles, tables) throughout each patient care area are to be disinfected by wiping with Wescodyne three times each day: at the beginning of each day before patients are seen, during the morning session, and at the end of the day. The chief technician in each area is responsible for implementing and documenting the disinfection efforts. Hands must be washed after contact with instrument surfaces contaminated by eye secretions.
(4) Medication distribution: All dilating and other diagnostic drops are to be discarded at the declaration of Condition Red. Drops are to be discarded daily in the ER and twice per week in the Resident and Faculty Clinics.
(5) Employee furloughs: Infected employees are not to work in any patient care areas for 14 days from the time of onset of symptoms. This includes employees who work in patient care areas but do not have direct patient contact. After presenting to an ophthalmologist for evaluation, employees with possible viral conjunctivitis will be relieved from duty for 3 days, after which they will undergo another ophthalmologic assessment. Employees with continuing clinical evidence of infection will then be relieved from further duty until 14 days after onset. Viral cultures for adenovirus are to be obtained from employees evaluated by the professional staff.

*Outbreak of September/October 1991*
Infection control measures were implemented on September 25, 1991. One week later, on October 3, 1991, two nosocomial cases of EKC were identified at the Institute, and the DHMH was notified by the ICP. The author authorized that the Institute go to a Condition Red.

*Investigation of the Outbreak of September/October 1991 by the DHMH.* The DHMH investigated the outbreak of September/October 1991 by performing environmental and epidemiologic investigations as well as a laboratory surveillance.[89,90] In cooperation with the ICC, the DHMH identified 38 cases of nosocomial and 103 cases of community-acquired EKC.
• Environmental investigation. The DHMH visit on October 4 revealed that many of the ICPPs were not being enforced. A Red Eye Room was

available but was found locked, and when it was opened, inadequate supplies for hand washing were found. There was no apparent decrease in the use of tonometry. Nineteen patients diagnosed with nosocomial EKC had undergone tonometry. Aseptic techniques for disinfecting pneumotonometers appeared to be adequate, with use of sterile disposable sheaths to cover the probe. The pneumotonometer tips were not cleaned at the end of the day or between patient examinations. The DHMH found that the physicians were using the latex sheaths instead of disinfection. However, the nursing staff noted that the physicians often placed the sheath on the tip without changing gloves after manual contact with a patient's eyes. In addition, previously recommended disinfectants were thought to be too caustic for the plastic tips. Routine disinfection of the Goldmann tonometer tips was not done. Routine discarding of all open ophthalmic solutions at the end of the day, however, was being practiced.

A follow-up visit 2 weeks later demonstrated marked improvement in the implementation of the ICPPs. The Red Eye Room was noted to be routinely used for presumed conjunctivitis patients. Adequate equipment and supplies were present. Tonopen tonometry with the disposable tips had replaced pneumotonometry for routine use. Slit lamps were cleaned with Wescodyne solution after each patient examination. Wescodyne disinfection of applanation tips in the clinic was routinely used.

• Epidemiologic investigation. Using the case definitions described in the Material and Methods section, 34 nosocomial and 103 community-acquired cases of EKC were identified by the ICC and DHMH. Fifteen nosocomial cases were found to be related to exposure in the emergency department and 19 were related to exposure in the resident clinic. On the basis of the number of patient visits per month, the attack rate was found to be 1.8% in the emergency department and 0.4% in the clinic for the period of the outbreak. Thirty-one nosocomial cases in the outbreak of September/October 1991 were identified (Fig 1). Community-acquired cases demonstrated sharp increases during this period. Nosocomial EKC cases by date of presumed exposure showed an increasing number of affected patients (Fig 2). EKC cases with known single exposure indicated that the median incubation period was about 10 days (Fig 3). Overall in 1991, two documented outbreaks occurred (Fig 4).

The case-control study by the DHMH and the ICC focused on these risk factors: age, diagnosis at initial visit, procedures, physician, and examination room. Results (Table IV) indicate that tonometry of any type was borderline significant. There appeared to be a high level of transmission from one clinic room on a particular day. Seven patients were examined by a particular physician in this room, and five developed EKC within 2

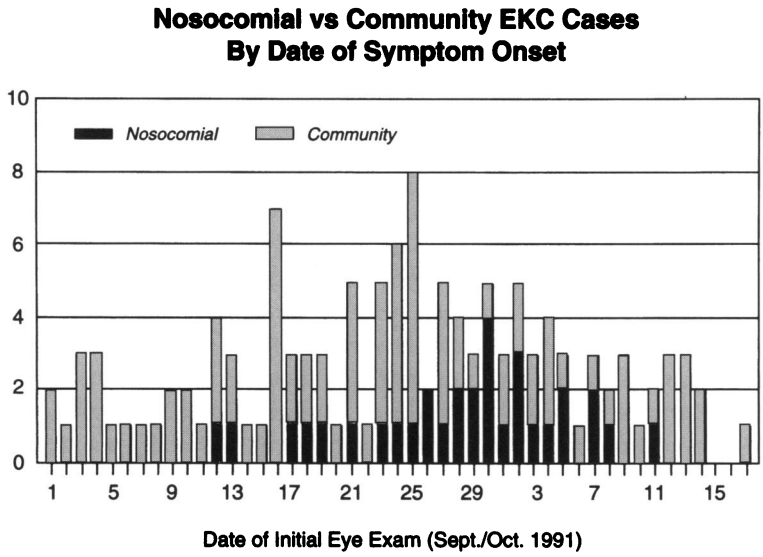
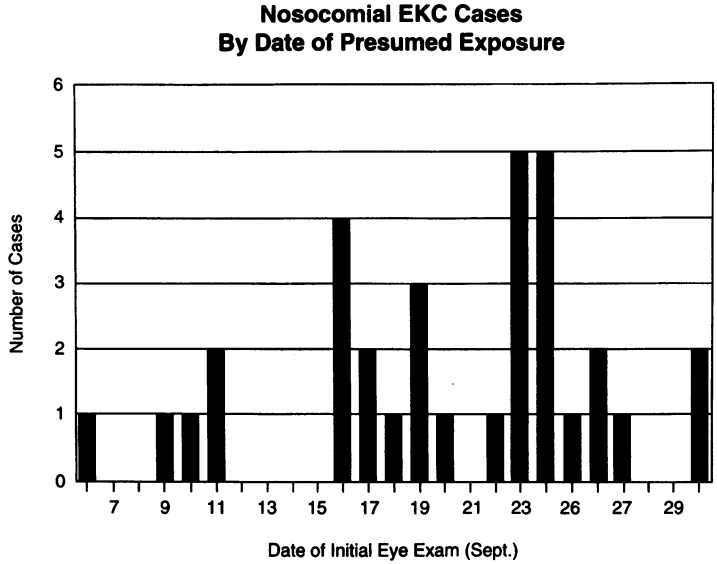



FIGURE 1

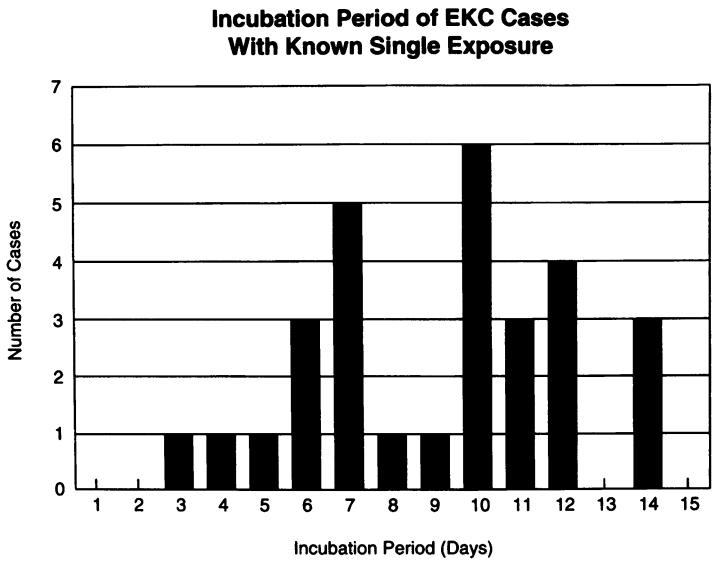
Number and time distribution of community and nosocomial cases of EKC during epidemic of September/October 1991.




EKC outbreak Oct. 1991

FIGURE 2

Number of nosocomial cases of EKC by date of presumed exposure demonstrating increasing number of affected patients with time into the epidemic.




Outbreak Oct. 1991

FIGURE 3

EKC cases during second epidemic of 1991 with known single exposure, indicating that median incubation period was about 10 days.

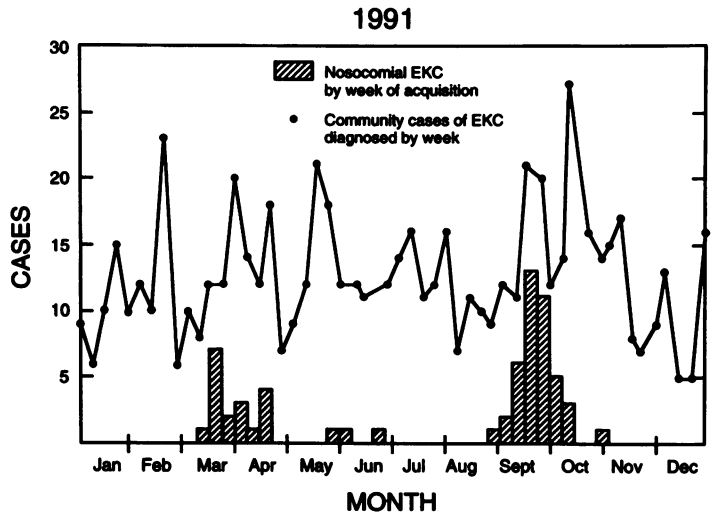



FIGURE 4

Two epidemics were noted in 1991. Unusually large numbers of community-acquired cases were noted during second epidemic.

TABLE IV: COMPARISON OF RISK FACTORS FOR EKC TRANSMISSION*

| RISK FACTOR | EXPOSED GROUP CASES (N=32) % | EXPOSED GROUP CASES (N=63) % | P VALUE |
|---|---|---|---|
| **Age** | | | |
| Child (0-19) | 15.6 | 19.1 | |
| Adult (20-59) | 40.6 | 44.4 | |
| Elderly (60+) | 34.4 | 30.2 | |
| Unclassified | 9.4 | 6.3 | |
| **Diagnosis** | | | |
| Intraocular problem | 25.0 | 15.9 | |
| Glaucoma | 31.3 | 27.0 | |
| Lid problems | 3.1 | 6.3 | |
| Eye surface defects | 25.0 | 28.6 | |
| Other extraocular+ | 9.4 | 9.5 | |
| Optic nerve/vision | 6.3 | 12.7 | |
| **Procedures** | | | |
| Slit-lamp examination | 81.3 | 84.1 | 0.72 |
| Fundoscopy | 56.3 | 88.9 | 0.70 |
| Tonometry (any type)≠ | 90.6 | 76.2 | 0.09 |
| Applanation | 40.6 | 44.4 | 0.72 |
| Pneumotonometry | 34.4 | 20.6 | 0.15 |
| Unknown type | 18.8 | 14.3 | 0.57 |
| **Physician** | | | |
| 1 | 18.8 | 12.7 | |
| 2 | 6.3 | 7.9 | |
| 3 | 12.5 | 14.3 | |
| 4 | 6.3 | 9.5 | |
| 5 | 9.4 | 6.3 | |
| 6 | 3.1 | 6.3 | |
| 7 | 0.0 | 9.5 | |
| 8 | 0.0 | 1.6 | |
| 9 | 6.3 | 4.8 | |
| 10 | 3.1 | 4.8 | |
| 11 | 0.0 | 3.2 | |
| 12 | 3.1 | 1.6 | |
| 13 | 15.6 | 3.2 | |
| 14 | 0.0 | 4.8 | |
| 15 | 0.0 | 0.0 | |
| 16 | 15.6 | 9.5 | |
| **Room** | | | |
| 1 (ER) | 40.6 | 38.1 | |
| 2 (glaucoma clinic) | 3.1 | 1.6 | |
| 3 | 3.1 | 1.6 | |
| 9 | 3.1 | 3.2 | |
| 13 | 6.3 | 7.9 | |
| 15 | 0.0 | 6.4 | |
| 17 | 9.4 | 7.9 | |
| 19 | 6.3 | 15.9 | |
| 21 | 0.0 | 3.2 | |
| 23 | 31.3 | 11.1 | |

* Second epidemic of 1991.
\+ Inflammation, dryness, tearing, foreign body.
≠ Borderline significance.

weeks. A comparison was made between the nosocomial and community-acquired cases for age, symptoms, diagnosis, knowledge of exposure, and viral identification (Table V). Six faculty cases were also identified by the ICP. The source of this infection was thought to be an emergency department patient with EKC who was brought to the faculty practice. One faculty member developed EKC. Two visitors in the waiting area also developed EKC, even though they had not had an ophthalmologic examination.

• Laboratory investigation. Fifty-eight cultures were collected from patients suspected of having EKC. Only adenovirus type 8 was isolated from nosocomial cases (Table VI). Cultures from most community-acquired cases also grew adenovirus type 8, but there were three cases of type 19.

*DHMH Recommendations for Infection Control Following September/October 1991 Outbreak.* The following recommendations were made by the DHMH:

• Routine use of the Red Eye Room at all times for all patients with red eyes or suspected infections.

• Hand washing with soap and hot water for at least 10 seconds before and after each patient.

• Disinfection of instruments (eg, slit lamps, funduscope, tonometers) by wiping all handles, knobs, and tables with Wescodyne solution or other effective disinfectant. Ideally, this should occur after each patient exmination at all times, but it is mandatory when the physician has touched a patient's eye secretions or during nosocomial outbreaks and is recommended during times of increased numbers of community cases. At a minimum, disinfection should be done twice daily. Areas of instruments that touch patients' eyes must be disinfected after each patient examination.

• Routine use of pen tonometers in the emergency department with the use of disposable tips that come in contact with the patients' eyes. Discontinue the use of pneumotonometers unless disinfection of tips between patients and routine use of sterile sheaths with aseptic handling can be assured.

•Routine disinfection of applanation tonometer tips by soaking in Wescodyne solution for 10 minutes or by another effective disinfection protocol.

• Avoidance of all forms of tonometry on patients with red eyes unless absolutely medically indicated.

• Discarding of all ophthalmic solutions that contact a patient's eye.

• Use, if possible, of a separate waiting area for patients with red eyes, especially when the number of community cases appears to be high.

TABLE V: COMPARISON OF CHARACTERISTICS IN NOSOCOMIAL AND COMMUNITY-ACQUIRED EKC*

| CHARACTERISTICS | NOSOCOMIAL CASES (N=32) % | COMMUNITY CASES (N=99) % |
|---|---|---|
| **Symptoms/signs** | | |
| Fever | 0.0 | 0.0 |
| Sore throat | 6.0 | 1.0 |
| Cough | 3.0 | 3.0 |
| Swollen lymph nodes | 50.0 | 41.4 |
| **Diagnostic label** | | |
| Adenovirus | 3.1 | 7.1 |
| EKC | 3.0 | 4.0 |
| Follicular conjunctivitis | 62.5 | 36.4 |
| Viral conjunctivitis | 31.3 | 47.5 |
| Other | 0.0 | 4.0 |
| **Age of patients** | | |
| 0-9 | 3.0 | 8.1 |
| 10-19 | 12.5 | 4.0 |
| 20-29 | 3.1 | 33.3 |
| 30-39 | 15.6 | 17.2 |
| 40-49 | 12.5 | 8.1 |
| 50-59 | 9.4 | 8.1 |
| 60-69 | 15.6 | 8.1 |
| 70+ | 18.8 | 1.0 |
| Unknown | 9.4 | 2.0 |
| **Known community exposure** | 3.1 | 12.1 |
| **Virus isolation** | | |
| Adenovirus 8 | 37.5 | 9.1 |
| Adenovirus 19 | 0.0 | 3.0 |
| No growth | 6.3 | 29.3 |
| Not done | 53.1 | 57.6 |
| Pending | 3.1 | 1.0 |

* Second epidemic of 1991.

TABLE VI: VIRAL CULTURE FROM EKC OUTBREAK (SEPT 1991)

| CASE CLASSIFICATION | NO GROWTH | ADENOVIRUS 8 | ADENOVIRUS 19 | OTHER | TOTAL |
|---|---|---|---|---|---|
| Nosocomial | 2 | 12 | 0 | 0 | 14 |
| Community | 29 | 9 | 3 | 0 | 41 |
| Faculty practice | 0 | 2 | 0 | 0 | 2 |
| **Totals** | **24** | **9** | **2** | **0** | **58** |

- Notification of the City Health Department in the event of two or more nosocomial cases of viral conjunctivitis in 1 week.
- Timely delivery of eye cultures for adenoviral typing.

The recommendations of the DHMH were in effect through the policy and procedures issued September 25, 1989, except for the recommendation that routine disinfection should occur after each patient examination at all times, including wiping all handles, knobs, and tables with Wescodyne. The ICC considered this recommendation unworkable, since it would place a burden on the technical support staff and would seriously impair patient flow. The DHMH ultimately agreed, and disinfection policy was amended to be mandatory after examination of each patient suspected of having infectious conjunctivitis and at three times during the day as specified in the ICPPs.

*Outbreaks in 1992*

In August 1992, two nosocomial cases of EKC were reported to the ICP, and the Institute went to Condition Red. The epidemic was confined to seven patients from the emergency department and one first-year resident physician (Fig 5). No other cases occurred within the Institute. A retrospective review of the outbreak revealed that some at the Institute, including a number of the resident staff, were not aware of the Condition Red until a full 4 days had passed. The ICC formulated a disaster control notification tree (Fig 6) that when implemented would theoretically alert the entire Institute within 1 day.

*Outbreaks in 1993*

No epidemics of EKC occurred in 1993 (Fig 7), the first time this had happened since record keeping of outbreaks at the Institute began in 1984. Five cases of EKC met the definition for nosocomial disease by virtue of

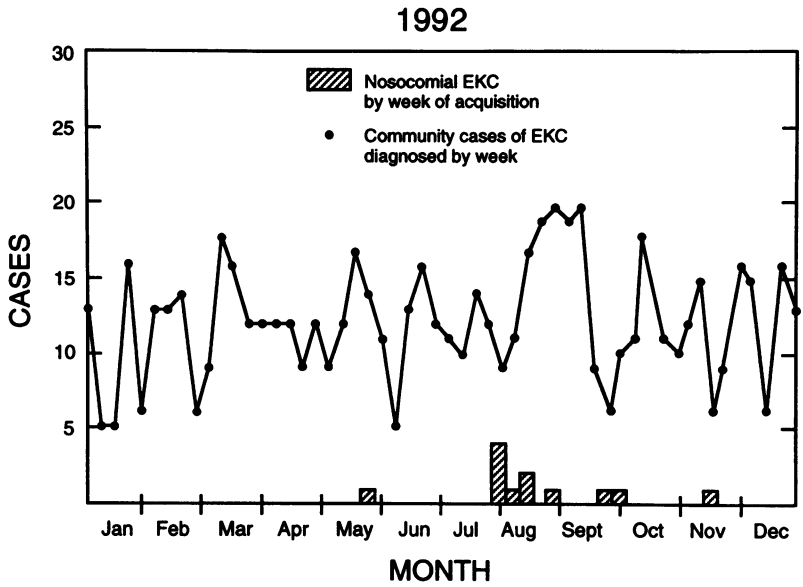



FIGURE 5

One smaller epidemic was noted in 1992. It occurred in emergency department and involved one physician.

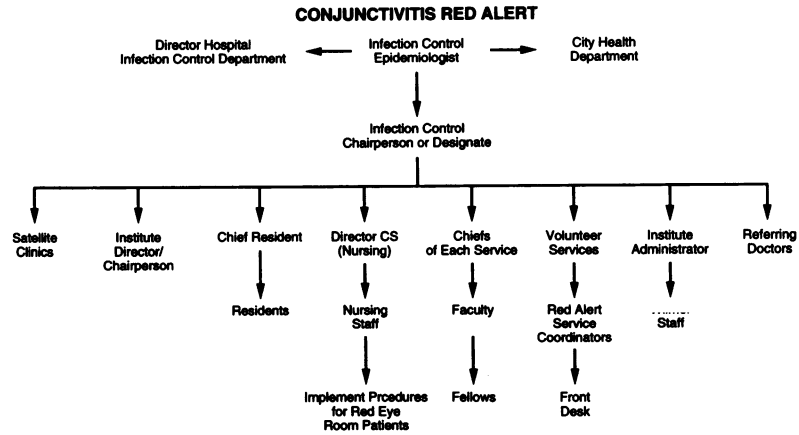



FIGURE 6

Disaster alert plan instituted after epidemic of 1992. Plan was amended to include satellite clinics and referring physicians after epidemic of 1995.

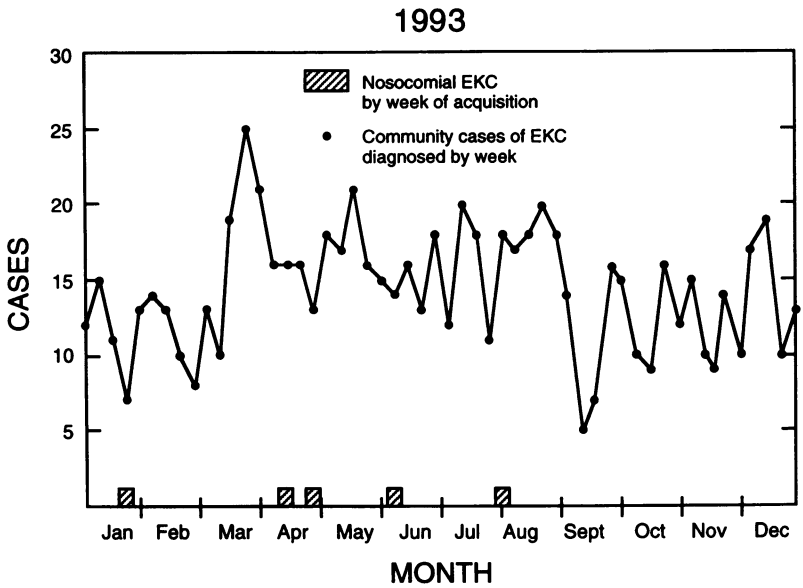



FIGURE 7

No epidemics were noted for 1993. This was first time since 1984, when formal record keeping of outbreaks of EKC began, that no epidemic during a 1-year period occurred at the Institute.

the patient having visited the Institute within the preceding 21 days. These may have been true nosocomial cases or could represent patients with community -acquired disease who coincidentally visited the Institute during the requisite period.

In March 1993, over 25 community-acquired cases of EKC presented to the emergency department. The Institute went to Condition Red per the Disaster Control Tree. A follow-up 24 hours later revealed that the notification system had worked well, and few staff were unaware of the Condition Red. Several patients complained about inadequate information explaining the limited access to the clinic and asked for more detail about the need for examination in the Red Eye Room. The ICC formulated a statement that the triage nurse used as a guide for instructing patients entering the Institute during a Condition Red.

The ICP reported in April and August 1993 that residents' red eye patients were often listed with a differential diagnosis that included EKC, allergic conjunctivitis, and blepharitis. The number of reported cases of EKC was thought to be inappropriately high owing to inclusion of other causes of a red eye. The residents were given a special lecture on clinical signs and symptoms of a red eye, especially EKC versus allergic disease,

and the need to distinguish among these diseases and make a clinical diagnosis. The number of ambiguous diagnoses dropped (Fig 7). "Red eye" lectures are now given to the beginning residents in July and at other times when the ICP reports that diagnoses are reported as differentials with no further work-up.

*Outbreaks in 1994*

No outbreaks of nosocomial EKC were identified in 1994 (Fig 8). The number of community cases approached 20 several times during the year, but no spread occurred within the Institute. Five isolated nosocomial cases were noted in both 1994 and 1993, but no other cases developed. Again, these cases may have been chance occurrences of community -acquired EKC in patients who happened to have made a clinic visit to the Institute. Alternatively, these may have been true nosocomial cases that, owing to rigorously enforced ICPPs, never spread further.

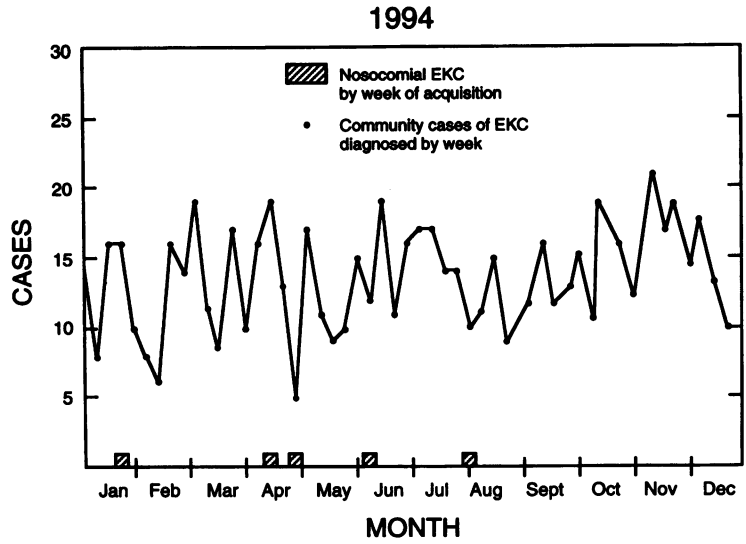



FIGURE 8

No epidemics were noted for 1994.

*Outbreaks in 1995*

On September 10, 1995, three cases of nosocomially acquired EKC were reported to the author involving the cornea and external disease service.

EKC epidemics in the community were also reported by referring physicians. A marked increase in the number of community-acquired cases of EKC were also seen and recorded in the Red Eye Room (Fig 9). The Institute went on Condition Red. Twelve cases were identified during the epidemic (Fig 9).

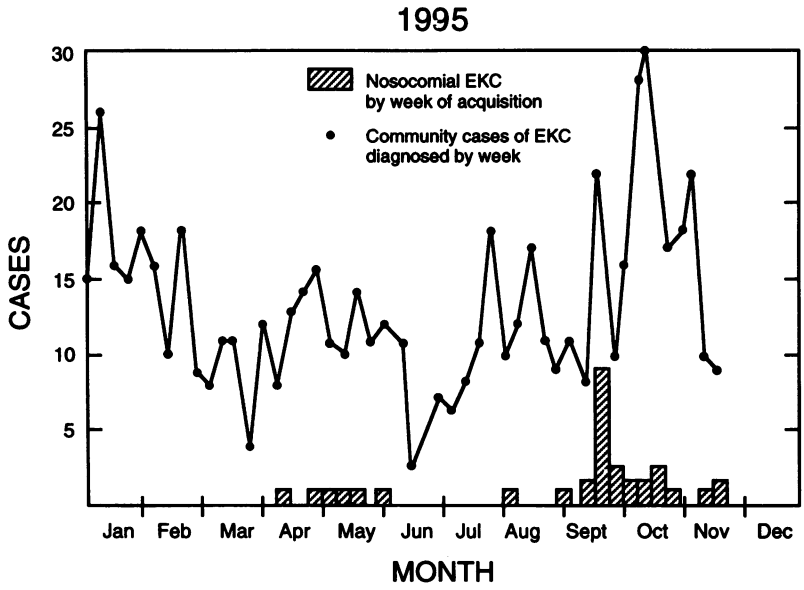



FIGURE 9

One outbreak was noted in 1995. It occurred on Cornea and External Disease Service as result of a technician improperly handling a pneumotonometer and an infected patient, in violation of ICPPs.

An epidemiologic investigation determined that the probable cause of the epidemic was a violation of one of the protocols of the ICCPs by a technician. The index patient (patient X) was a recent corneal transplant patient who had been diagnosed with a bacterial corneal ulcer. Because his red eye was presumed to be due to an underlying bacterial infection and to the administration of fortified topical antibiotics, a diagnosis of EKC was not suspected. The patient requested to have the first appointment of the day for his follow-up appointments. For 7 consecutive follow-up days (Fig 10), patient X was seen as the first or one of the first patients of the day, always by the same technician. When interviewed, the technician reported that all of the ICPPs were followed, including hand washing, but that the pneumotonometer was used without the protective probe caps. In

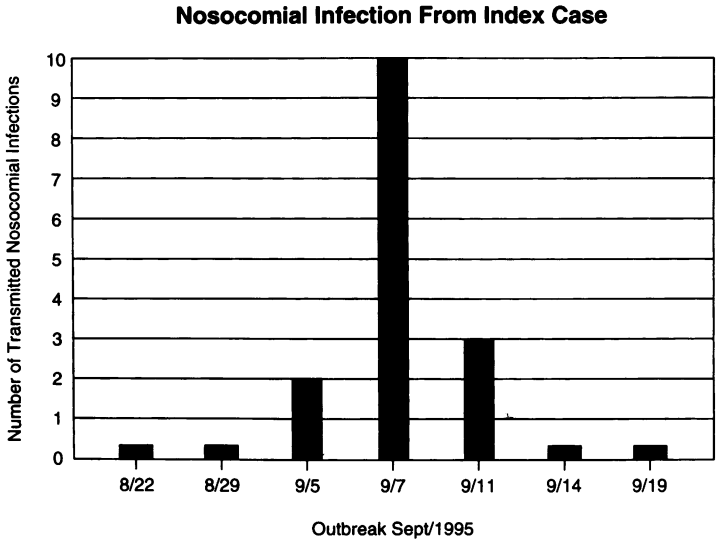



FIGURE 10

Number of nosocomial infections by dates from index case during epidemic of 1995. Patient was identified as source of inoculum responsible for infecting subsequent patients by the technician improperly handling a pneumotonometer. Length of time the index patient was able to transmit the disease provides some insight into how long this strain of adenovirus 8 remains infective.

a number of patients who subsequently followed patient X and underwent pneumotonometry, epidemic keratoconjunctivitis developed. Those who did not have tonometry did not develop EKC. On three consecutive visits, patient X was implicated as the inoculum source for the pneumotonometer that was involved in the inoculation of all subsequent patients by the same technician. Two patients developed EKC on a visit on September 5, nine patients on September 7, and three patients on September 11 (Fig 10). No patients were infected by patient X on visits of August 22, August 29, September 14, and September 19, even though the same technician reported using identical tonometry techniques. Patient X was culture-positive for adenovirus type 8, as was his wife and all the other cultured nosocomially infected patients.

One patient was seen at a satellite clinic and was implicated in a mini-epidemic of three other patients, prompting satellite physicians to request notification of when the Institute was on Condition Red. Appropriate satellite personnel were invited to attend ICC meetings so that mechanisms for the implementation of ICPPs at satellite clinics could be suggested. In addition, one referring physician had a patient who had been

seen at the Institute and had been nosocomially infected. This referring physician also requested notification of a Condition Red alert by the Institute. Subsequent communication with a number of referring physicians indicated that they, too, would like to be alerted when an epidemic was declared. The author requested that referring physicians, when possible, call to communicate an epidemic of EKC in the community or their office practices.

*Statistical Comparison Before and After Implementation of ICPPs*

From 1984 through 1995, the epidemic rate (number of epidemics/total number of patient visits) and the affected patient rate (number of affected patients/total number of patient visits) were calculated with 95% confidence intervals based on a Poisson distribution. The test of significance in epidemic rate and affected patient rate before (1984 through 1991) and after (1992 through 1995) ICPPs and using the chi-square test of observed versus expected were, respectively, $P<.01$ and $P<.01$ (Table I) These results indicated that the implementation of ICPPs decreased the number of epidemics and the number of affected patients.

## DISCUSSION

The implementation of ICPPs designed to prevent and control nosocomial outbreaks of EKC at the Wilmer Institute, decreased the incidence of outbreaks of EKC ($P<.01$) and the number of nosocomially infected patients ($P<.01$). The implementation of the ICPPs, only two epidemics occurred during the 4 years of the study. A review of documented outbreaks for the preceding 8 years (1984 through 1991) at the Institute showed that at least one and as many as three outbreaks occurred per year. The ICPPs have evolved into an effective means to decrease the number of outbreaks and the number of affected individuals of EKC for this particular institution. Although several reports of institutional outbreaks of EKC have described infection-control measures that eventually controlled an outbreak well under way, this study provides a set of policies and procedures of how large teaching eye institutions may effectively decrease nosocomial epidemics of viral conjunctivitis.[79,84-87] Although the applicability of these ICPPs to satellite clinics and ophthalmic offices has yet to be tested, modification and implementation of these infection-control measures may reduce the number of nosocomially infected patients in these settings.

The history of EKC at the Wilmer Institute began in 1948, when Maumenee discussed his first cases evaluated in Baltimore.[88] As Director

of the Institute from 1955 through 1979, Maumenee recalled that at least one, sometimes two, and occasionally three outbreaks would occur a year, usually originating in the Glaucoma or Cornea Services. In 1980, outbreaks were studied and reported in the minutes of the Infection Control Department of the Hospital. In every year between 1984 and 1992, a documented outbreak of EKC occurred at the Institute. By happenstance, the initial policy and procedures were implemented during the beginning of an outbreak in September 1991. Even though the effectiveness of these policies in preventing a nosocomial outbreak could not be judged, an evaluation of the measures to control the outbreak was performed by the ICC and the DHMH of the State of Maryland. Suggested modifications by the DHMH, particularly concerning the Red Eye Room, were implemented. The next outbreak was confined to one resident physician and seven patients. The policy was modified to include a disaster notification plan to speed the implementation of a Condition Red.

Since the outbreak in August 1992, no further epidemics occurred at the Institute for 3 years until an epidemic occurred on the Cornea and External Disease Service during a quite severe concurrent epidemic in the community. An epidemiologic investigation identified the source of the epidemic as a technician who failed to follow the ICPPs regarding correct pneumotonometry sterilization. The index case was a patient whose red eye was presumed to be due to a bacterial corneal ulcer and topically applied fortified antibiotics. A diagnosis of EKC was not suspected until the patient was implicated in an epidemic. Because the patient requested the first appointment of the day and because he was tested on each successive visit by pneumotonometry with improper sterilization, the technician effectively inoculated successive patients who needed tonometry with adenovirus 8. In effect, this epidemic involving this index case demonstrated the ability of this adenoviral strain to inoculate and infect successive patients over a specified time period. The study of this epidemic gives some indication of the length of time—about 7 days—that this particular strain of adenovirus remains infective.

Isolated nosocomial cases have been identified, five during 1993, five during 1994, and six during 1995. These patients met the definition of a nosocomial case by developing the disease within 21 days of visiting the Institute. It is not known whether these patients contracted their disease at the Institute or had community-acquired disease and happened to visit the Institute during the specified time period. However, no epidemics involving a cluster of patients developed from these isolated cases. If these isolated nosocomial cases are real, it would indicate that the ICPPs are playing a substantial role in preventing the development of an epidemic.

The policy and procedures were divided into two levels of alertness. Condition Yellow is a set of policies designed to prevent the occurrence of an outbreak at the Institute. Condition Red represents another layer of modified policy and procedures to bring an epidemic under control once it has begun and to keep additional localized epidemics from gaining a foothold in other areas of the Institute, in satellite offices, and/or in referring physicians' offices. Recognition of the success in controlling EKC at the institutional level has compelled both satellite offices and referring doctors to request notification of a Condition Red in order to be on alert for a possible epidemic in their offices or clinics. The policies and procedures formulated and instituted in Condition Red had long been recognized as important in preventing the spread of nosocomial disease. Cockburn and associates[33] first recognized that contaminated physicians, as well as their instruments, were likely sources for transmitting the disease. Routine hand washing was recommended by Thygeson,[73] as well as disinfection of instruments, discarding of contaminated medications, and isolation of infected patients. Hendley[91]discussed the value of routine hand washing and the effectiveness of virus removal with a 10-second hand wash with or without soap. Many doctors wash their hands after examining a patient to remove microorganisms acquired from that patient.[92] Hendley pointed out, however, that the correct time for physicians to wash their hands is before examination of the patient so that pathogens derived from the doctor and from other patients can be removed.

Studies of a few outbreaks of EKC demonstrated the effectiveness of routine infection-control measures in resolving an epidemic.[71-74,79] However, the reports of other large institutional outbreaks concluded that routine infection control measures were not effective unless the strict identification and isolation of the infected patient were concurrently performed.[85-87] The creation of a Red Eye Room requires the allocation of space and resources that would otherwise be used for routine patient care. Even though these resources are not routinely used, their availability for use is mandatory for successful infection control of EKC.

It was the aim of the ICC not only to contain an outbreak but, if possible, to prevent outbreaks of EKC in the Institute. Condition Yellow was created as a baseline level of alertness to be in effect during all nonepidemic periods. The measures were designed to be rigorous enough to prevent EKC from spreading within the Institute, yet sufficiently flexible and unobtrusive to allow for the routine evaluation and normal flow of patients. The policies and procedures of Condition Yellow were based on the recommendations that had proved effective in controlling an outbreak. The Red Eye Room was maintained during Condition Yellow for the iso-

lation and evaluation of community -acquired cases of EKC that presented to the Institute. The isolation of patients with EKC prevented the contamination of waiting rooms, staff, and physicians. Indeed, in the study of one of the outbreaks at the Institute, two relatives accompanying patients had acquired the disease during an outbreak, presumably while sitting in a contaminated waiting room. Because some patients may be subclinically infected or in the early stages of the disease, routine hand washing before examining any patient was stressed for all physicians and technicians, and routine disinfection of all instruments was performed by physicians and technicians.

Gloves have been recommended for physicians examining patients as a way of preventing the transmission of disease.[87] The ICC considered routine use of gloves but concluded that physicians were likely to forget that gloves had become contaminated and that equipment and instruments in the room would become contaminated as they performed other routine procedures. Instead, a concerted effort to convince physicians and technicians to wash their hands before and after examining patients was attempted by biannual infection-control seminars and by announcements at conferences where local ophthalmologists examine patients.

An important aspect of the ICPPs that required considerable cooperation among the ICC, the University Health Service, and the Occupational Health Service of the Hospital was the formulation of a unified work furlough policy for Hospital and University employees who were suspected of having viral conjunctivitis. Considerable evidence supports the removal of an infected employee while contagious, whether it be a physician, nurse, or staff member who has contact with patients or visitors. However, not all employees with a red eye have EKC, and a furlough for 14 days is not always appropriate. An employee with a red eye and possible conjunctivitis should be evaluated in all cases by a physician. If viral conjunctivitis is suspected, the employee is to be reevaluated, at which time viral cultures and/or increasing clinical signs might permit a definitive diagnosis. The employee with resolved or resolving (no discharge) clinical signs should return to work. The employee with a positive culture or definitive clinical signs of EKC is to be furloughed for 14 days if an epidemic is under way or until symptoms and drainage resolve in a nonepidemic period. Importantly, before an employee can return to duty, a Return to Work Release Form must be obtained from a physician.

Adenoviral isolates of types 8 and 19 are recoverable from plastic and metal for up to 7 weeks.[93] These hardy viruses may survive for a considerable time in contaminated waiting rooms and on instruments. The tonometer, whether a Schiotz, Goldmann, pneumotonometer, or Tonopen,

has been implicated in a number of outbreaks. Because these instruments come in direct contact with the eye, inoculation of a susceptible individual can easily occur. For each type of tonometer, specific disinfection recommendations have been made. For pneumotonometers, the use of disposable sheaths has worked well.[94] Disinfection of the pneumotonometer tips with an alcohol wipe may not be acceptable.[82] For Goldmann tonometer tips, a number of disinfecting mechanisms have been shown to be effective: soaking in sodium hypochlorite (1:10), hydrogen peroxide 3%, or isopropyl alcohol 70%, or use of an alcohol-soaked pad or a water-moistened gauze.[95-99] Whether disinfecting a Goldmann tonometer tip or a pneumotonometer, the examining physician must thoroughly wash hands prior to handling the patient or the instrument lest the instrument become contaminated. Also, the disinfected instrument be thoroughly rinsed, because the patient who is examined and comes in contact with an unrinsed instrument may suffer a corneal chemical burn.[100]

From the earliest clinical descriptions at the turn of the century, EKC has remained a distinctive disease characterized by acute follicular conjunctivitis followed by central subepithelial infiltrates.[1-5] Although several diseases are similar in presentation (herpetic keratoconjunctivitis, pharyngoconjunctival fever, acute hemorrhage conjunctivitis), only certain adenoviral types consistently produce outbreaks of disease with these two clinical signs. Adenoviruses responsible for EKC have certain biologic properties that contribute to the characteristic epidemiology of the disease.[45-50] First, the virus reproduces in relatively large numbers, but a small percentage of the virions are infective. Thus, there is low spontaneous transmissibility of the disease to the general population with low levels of immunity, leaving large numbers of susceptible individuals. In studying many outbreaks of EKC, it becomes apparent that the disease has a low attack rate among family members, yet it can become an explosive epidemic in the eye clinic. Direct inoculation of the eye is a most effective method of producing disease, and inoculation can be provided by the contaminated physician, instruments, or medications. Indeed, there is evidence that direct inoculation of the human eye may be the only way the disease can produce symptomatic disease, because even direct subcutaneous injection of the virus does not produce disease in volunteers.[50]

Although EKC is distinctive in its clinical signs and symptoms, it is caused by several adenoviral types and not others. It is its epidemic nature that makes the disease such a troublesome conjunctivitis in the eye clinic setting. Certainly, the usually transitory yet debilitating subepithelial infiltrates are an additional reason to protect susceptible patients from acquiring the nosocomial disease. However, there are other types of viral infec-

tious conjunctivitis that cause epidemic disease from which the unsuspecting patient should be protected. These diseases include pharyngoconjunctival fever and enterovirus 70. Both these types of viral epidemic conjunctivitis have been associated with adenoviral type 8 disease.[86,101,102] Any infection-control measures should certainly include procedures appropriate for these viral diseases. In our study of epidemic viral conjunctivitis from 1989 through 1995 with viral cultures, however, only adenoviral types 8, 19, and 30 have been identified. Identification of these patients is the responsibility of the treating physicians and technicians. Fortunately, the presenting clinical sign of EKC, pharyngoconjunctival fever, and enterovirus 70 is an acute conjunctivitis, which is the entry requirement for the Red Eye Room. The resident makes a differential diagnosis according to the patient's history and clinical signs; a preliminary diagnosis is made and is confirmed by viral culture or other clinical findings on subsequent follow-up. Pharyngoconjunctival fever has been identified in a number of pediatric patients presenting to the emergency department and to various subspecialty clinics; however, no nosocomial outbreaks have been identified at the Institute. Sporadic cases of culture-proven acute hemorrhage conjunctivitis have been diagnosed, and again no outbreaks associated with enterovirus 70 have been detected. This particular disease is rare in the United States, but a number of outbreaks have been detected in the Caribbean Islands and in the Far East and Pacific Islands.[86,101-103] The possibility of an enterovirus 70 epidemic has to be considered, and the infection-control measures for adenoviral EKC may need amending if, for some as yet unknown reason, they prove to be inadequate.

In reviewing the viral isolates of cultures of staff and patients with EKC, only adenoviral types 8 and 19 were identified. In no case was type 37 cultured, an adenoviral type that is presumably a cause of worldwide disease.[68-72] In fact, no type 37 has ever been cultured from EKC cases at this hospital (M. Foreman, MD, personal communication, January 1995). It has been our experience, as reported by others, that adenovirus types 8 and 19 produce identical signs and symptoms of clinical disease.[56-57]

The effectiveness of the ICPPs is dependent on the ability of the residents to carry out properly the duties of the Red Eye Room (ie, to identify potential patients at risk for the disease, to make a proper diagnosis, and to distinguish among the various etiologies of a red eye). The level of alertness for the Institute is determined by the number of community-acquired cases logged and by the number of nosocomial cases identified by the residents. From time to time, the ICP in reviewing the log of EKC cases would note that one or more of the residents were not evaluating a patient for the specific signs and with the appropriate tests to make a spe-

cific diagnosis of a red eye. Often, merely a differential diagnosis (eg, EKC versus allergic conjunctivitis versus blepharitis) would be made with no further workup. This would cause confusion as to the actual number of community-acquired cases of EKC presenting to the Institute. These ambiguous diagnoses usually occurred in the spring or fall, when allergic conjunctivitis was common, or in July, when new, inexperienced residents were faced with making a diagnosis of a red eye. To help the residents, a mini-lecture on the differential diagnosis of a red eye is given at the beginning of a new academic year or when there appear to be difficulties as evidenced by the patient log.

The efforts geared toward prevention of EKC in this large Institute have brought an understanding to the faculty, residents, and staff that infection control procedures are effective and not a wasted effort. Another outbreak is inevitable, but with assessment and a critique of future outbreaks, further refinements of policy and procedures can be instituted so that the number of acquired cases of EKC at the Institute can be kept to a minimum.

The sine qua non for success, however, is the institution's willingness to change old practices and adopt new. To decrease the risk of an epidemic, hours of data collection supported by the concerted efforts of the state DHMH, the hospital infection control specialists, and the departmental infection control committee were needed to refine new policies and procedures. A nurse was assigned to intensive data monitoring. Faculty time and energy were focused on the problem, not only in association with committee meetings and document review and preparation, but with resident and physician education programs. Technicians and nurses were freed from other responsibilities to stand guard in the lobby during Condition Red alerts. Two Red Eye Rooms with adjoining waiting space were designated and kept free from other clinical use. Infected eye-care personnel were given furloughs where appropriate, and temporary replacement staff were hired. Ironclad adherence to the principles outlined in this thesis produced dramatic and gratifying results, but only with a strong institutional commitment from the hospital leadership and the department chairman as well as the rank-and-file employees of the Institute.

## SUMMARY

In this first prospective study of institutional outbreaks of EKC, the implementation of infection control policies and procedures was demonstrated to be an effective means of decreasing the number of EKC outbreaks ($P<.01$) and nosocomially infected patients ($P<.01$) for this particular insti-

tution. Outbreaks of EKC can be devastating to the everyday operation of a large teaching eye institute and can bring much pain and suffering to patients and staff. The history of EKC shows this disease to be well suited for transmission by the physicians and staff in an eye clinic setting. Routine infection control measures (hand washing, instrument disinfection, medication disposal, and employee furlough) are effective in bringing an ongoing epidemic under control when combined with isolation of infected patients.

To minimize the potential for an outbreak in an institutional setting, a baseline set of infection control procedures should be practiced daily by physicians and staff, and measures should be taken to identify patients and staff at risk for spreading disease. The use of two levels of infection control procedures (Condition Yellow for everyday, routine procedures, and Condition Red for procedures at the time of a pending or real epidemic) has successfully decreased the number of EKC epidemics and the number of affected patients at the Wilmer Institute. These policies and procedures may help serve as a model for other large teaching eye institutions to curb outbreaks of this nosocomially acquired disease.

**ACKNOWLEDGEMENTS**

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